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PROVISIONAL APPLICATION COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION under 37 CFR 1.53 (c).

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INVENTOR(S)/APPLICANT(S)

LAST NAME	FIRST NAME	MIDDLE INITIAL	RESIDENCE (CITY AND EITHER STATE OR FOREIGN COUNTRY)
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TITLE OF THE INVENTION (280 characters)

A PROSTHETIC DEVICE FOR TRANSARTERIAL CATHETER-BASED IMPLANTATION INTO AN OBSTRUCTED AORTIC VALVE DESIGNED TO MINIM HEAD LOSS BY PRESSURE RECOVERY AND SUITABLE FOR USE WITH AND WITHOUT AN ATTACHED VALVE PROSTHESIS

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☒	Specification	Number of Pages	7	☒	Applicant claims "small entity" status. ☐ "Small entity" statement attached.
☒	Drawing(s)	Number of Sheets	12	☐	Other (specify)

METHOD OF PAYMENT *(check one)*

☒ A check or money order is enclosed to cover the Provisional filing fees ($Error! Reference source not found.)/($80.00)	PROVISIONAL FILING FEE AMOUNT ($)	80.00
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The invention was made by an agency of the United States Government or under a contact with an agency of the United States Government.

☒ No.

☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,
SIGNATURE _____ DATE July 8, 2003

TYPED or PRINTED NAME Joseph S. Presta REGISTRATION NO. *(if appropriate)* 35,329

☐ Additional inventors are being named on separately numbered sheets attached hereto.

PROVISIONAL APPLICATION FILING ONLY

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754363

A Prosthetic Device for Transarterial Catheter-Based Implantation Into an Obstructed Aortic Valve Designed to Minimize Head Loss by Pressure Recovery and Suitable for use With and Without an Attached Valve Prosthesis

1. Field of the invention

The present invention relates to a novel device for use in the management of cardiovascular diseases. More specifically, the present invention provides a transarterially-delivered prosthetic device for the treatment of aortic stenosis, combined aortic stenosis and aortic regurgitation, aortic regurgitation, and other valvular lesions.

2. Background and prior art

2.1 The problem of aortic stenosis and current treatment options

Aortic stenosis is the obstruction of outflow from the left ventricular chamber into the aorta caused by restricted opening of the aortic valve during cardiac contraction. The diminished aortic valve opening area (from normally 3 cm^2 to less than 0.5 cm^2 in severe cases) results in a significant pressure drop across the valve and normal cardiac output and aortic pressure can only be maintained at the expense of an increased intraventricular pressure. The high pressure which has to be generated by the left ventricular chamber results in increased wall tension and myocardial oxygen demand. Adaptive processes such as hypertrophy (compensatory increase in muscle mass) allow the heart to withstand this increased pressure load for some time, but ultimately, pump failure is inevitable.

In the majority of cases (and in more than 90% of all patients older than 65 years) aortic stenosis is caused by progressive fibrous and calcified degeneration of an originally normal valve, a process which is favored by hyperlipoproteinemia, arterial hypertension, and aging (acquired calcified aortic stenosis). The average survival of a patient with severe aortic stenosis and shortness of breath is less than two years. Since death may occur suddenly in a substantial portion of cases, some authors recommend preventive surgery even in asymptomatic patients, provided they are good surgical candidates.

Surgical results in the selected group of patients with isolated aortic stenosis are reasonable. Operative mortality in such patients is about 5%. However, most individuals with significant aortic stenosis are in their seventies and eighties. These patients have usually multiple comorbid risk factors, such as coronary artery disease, cerebrovascular disease, generalized atherosclerosis, renal failure, or diabetes. Consequently, surgical mortality and morbidity is substantial. Moreover, if the calcified aortic valve is replaced by a mechanical prosthesis, anticoagulation is mandatory to reduce thromboembolic complications, which exposes the patient to an increased risk of serious bleeding. Implantation of biological prostheses is usually preferred in the elderly, but surgically implanted biological valves may have a

suboptimal hemodynamic profile, because the suture ring on which the valve needs to be mounted reduces the space available for the valve itself. This poses a particular problem in women, were bioprostheses of a smaller size (which have to be used because of the smaller cardiac dimensions) may result in significant residual outflow obstruction.

2.2. Balloon-Dilatation

Because of the significant risk of elderly patients undergoing open-heart surgery on cardiopulmonary bypass - which includes death, disabling stroke, respiratory and renal complications - dilatation of the narrowed valve using balloon-catheters was hoped to provide an alternative to surgery. Unfortunately, because immediate results of the ballon dilatation are suboptimal (the average post-procedure opening area in the National Heart Lung and Blood Institute registry was 0.8 cm2), and recoil of the stenosis reoccurs within weeks and months in virtually all patients, outcome is as poor as in patients who do not undergo surgery. Balloon-dilatation is therefore only justified in patients with a clear contraindication to surgery or as a "bridging procedure".

2.3 Previously suggested stent-based valves for transarterial deployment (valved stents).

In analogy to the use of stents in coronary arteries it has been suggested to use (valved) stents in order to achieve a sufficiently large valve area and avoid elastic recoil and restenosis. In 1992, Andersen et al. reported their experience with a foldable porcine aortic valve (27 mm) sutured in an expandable stainless-steel stent. The valved stent was mounted on a 12F three-foiled balloon catheter, which fitted into a 41F introducer sheath. The valve was implanted in 9 pigs (5supracoronary implantations, and 4 subcoronary implantations). Only the subcoronary implantation with displacement of the native aortic cusps is a treatment option for aortic stenosis (the supracoronary implantation leaves the stenotic valve in place). However, subcoronary implantation resulted in two of the four cases in fatal occlusions of the coronary arteries which arise directly above (at the back of) the aortic cusps. Bonhoeffer et al. suggested the use of a vein segment containing a native biological valve from a bovine jugular vein. The valved stent was mounted on an 18-22 mm balloon-catheter front-loaded in a 16F Mullins long sheath and implanted in the pulmonary position, completely displacing the pulmonary cusps, which were pressed between stent and pulmonary artery wall with full deployment of the stent. However, this (similar) approach would necessarily result in coronary artery occlusion when undertaken in the aortic position.

Even when the stent is not deployed across the full area of the aortic annulus atheromatous deposits on the ventricular side of the aortic cusps may be pushed against the ostia of the coronary arteries causing severe coronary obstruction or embolization. Severe distention of a heavily calcified aortic valve to allow deployment of a sizeable stent may also cause embolization of calcium deposits from the valve or a tear in the valve resulting in significant aortic regurgitation. Furthermore, a large stent-valve may also interfere with surrounding structures such as the anterior mitral leaflet (causing damage to it or impairing its function), and - if protruding into the left ventricular outflow tract - the basal ventricular septum, which is usually hypertrophied in significant aortic stenosis.

In short, anatomy and pathology of the aortic root may only allow deployment of a smaller than optimal stent within the calcified valve, and the cross-sectional area of such a stent will probably be not be significantly greater than 1 cm^2 in most cases, which is roughly a third of a normal outflow tract area. Unfortunately, the main reason for the clinical failure of balloon-angioplasty was that more than 70% of the patients were left with an aortic valve area of less than 1.0 cm^2.

3. Current invention

3.1 The concept of the presented invention

The present invention is primarily directed to implanting a prosthetic device into a diseased aortic valve for use in the treatment of aortic stenosis in mammalian subjects. The device of the present invention comprises a straight segment (expandable stent) placed into the dilated aortic orifice and anchored using proximal (ventricular) and distal (aortic) ring-plates for secure and stable fixation as shown in Figure 7. Together with a smooth inlet-geometry which avoids flow contraction the straight segment (throat) minimizes flow-separation (Figure 7). Distal to the straight segment the device comprises a funnel-shaped tube with streamlined outflow geometry for maximal pressure-recovery. The end of the tube contains a foldable prosthetic aortic valve, preferably a biological prosthesis, sutured inside the tube (or attached by an alternative mechanism), with a valve opening area exploiting most of the cross-sectional tube area. The invention also provides a catheter-based method for implanting the pressure-recovering, valve-carrying device by mounting it onto a balloon-catheter fitted into an introducer-sheath (Figure 9)

The present invention recognizes that the maximum orifice area of an implantable aortic valve stent is necessarily confined by anatomical and pathological limitations and subsequent concerns about the safety of deployment. It is therefore aimed to reduce/prevent a permanent loss of pressure across any given cross sectional flow area of the stent. This will allow achieving a reasonable hemodynamic profile (low pressure gradients) even for relatively small-sized stents/valves as well as to optimize the hemodynamic profile (reduce pressure gradients even further) for larger stents/valves. The physical principles applied include pressure-recovery by streamlining the outlet geometry in order to avoid the occurrence of turbulence and kinetic energy dissipation as in a Venturi-meter.

The device will be provided in various sizes to accommodate different prosthetic sizes (e. g. 18 to 27 mm biological prostheses) so that patients of all possible height and body surface area can be treated. A typical diameter of the straight segment will be 1.3 cm (covering only 2/3 of the average outflow tract diameter of an adult); a typical length of the segment will be 0.5 cm; a typical length of the funnel-shaped tube will be 1.8 to 2 cm, with a typical angle alpha (widening angle, deviation from straight segment) of 12 to 25 °, since an angle α of 12 ° produces almost full pressure recovery for laminar flow. Example: if the straight segment has a diameter of 1.3 cm (cross-sectional area 1.4 cm^2), then a tube attached to this segment and widening with an angle α of 17° over a distance of 2 cm will have a diameter of 2.5 cm at its end (cross-sectional area 4.9 cm^2). Consequently, this device will be able to accommodate a 25 mm biological prosthesis at its end (in the aorta) with favorable hemodynamics, although throat size (straight segment within the valve) is only 13 mm in diameter.

3.2 Application of the physical principle of pressure recovery

By continuity, flow must accelerate at the orifice (increase in kinetic energy, dynamic pressure). Conservation of energy dictates that this is paralleled by a decrease in potential energy (static or lateral pressure). Most of the kinetic energy is dissipated into turbulence and cannot be reconverted into static pressure (Figure 1).

Streamlining the outlet geometry as in a well-designed Venturi meter by gradual expansion downstream of the throat eliminates flow separation in the decelerating portion of the device. Head losses are therefore reduced to a minimum (Figure 2). The principles of flow regulation in the cardiovascular system are quite similar to those in pipeline systems. Aortic pressure and cardiac output are regulated by the baroreceptor-system (Figure 3) with its stretch-receptors in the aorta and carotid artery. Any loss of pressure will lead to a centrally mediated increase in cardiac output until the preset systemic pressure is again reached. Because of this cybernetic loop any reduction in head loss achieved by a device (such as an aortic valve stent-prosthesis) with a streamlined, Venturi-tube-like (funnel-shaped) outlet geometry will therefore necessarily result in a reduction in left ventricular systolic pressure, i.e. in left ventricular work load (Figure 4).

3.4. Rationale for the design of the inlet-geometry

A stent protruding into the outflow tract will have the most unfavorable inlet geometry with a coefficient of contraction of 0.5. This means that the effective orifice area will be only 50% of the anatomic orifice area. In order to avoid flow contraction a smooth inlet geometry is required (Figure 5) and will be implemented.

3.5 Rationale for the design of the throat segment

In order to avoid flow-separation at the inlet, which may also decrease effective orifice size (Figure 6), a straight segment (stent) of a predefined length (throat length) will be introduced (figure 7). This part will be attached to a ring/plate (in addition to the one provided by the shape of the inlet) for secure and stable fixation, as well as for covering the space between the round stent and the triangular or irregularly-shaped native aortic valve opening area, thus avoiding significant regurgitation (Figure 7).

3.6 Position of the fully-deployed device

The fully deployed stent-based aortic valve prosthesis is displayed in Figure 8. The inlay drawing in the left upper hand corner represents a cross section through the device immediately above the native aortic valve ("aortic valve seen from above). The area of flow is shown in crimson red; the ring/plate (umbrella) for stabilization is shown in blue. There is ample space between the device and the ostia of the coronary arteries to provide for unobstructed blood flow. The distal end of the funnel-shaped device will preferably contain a (collapsible) biological prosthesis, but a combination with any other valve mechanism (ball-cage, disc-cage, tilting disc, bileaflet valve, check-valve) of a mechanical/synthetic type is possible. The diameter/cross-sectional area of the bioprosthesis will essentially represent the effective anatomical orifice area. The inlay drawing in the left lower hand corner represents a cross section through the device at its distal end containing a (bio)prosthesis. Because the bioprosthesis is positioned in the ascending aorta, frequently dilated in patients with significant aortic stenosis, an appropriately sized valve can be selected to address the patient's needs. In contrast, implantation of the bioprosthesis into the native valve

itself (or close to it), as suggested by prior art, would necessarily require selection of an undersized prosthesis due to the anatomical constraints detailed above and result in an unfavorable hemodynamic profile.

3.7 Mode of deployment

The collapsed system which includes an expandable stent (throat), a proximal umbrella (ring/plate) at the inlet, a distal umbrella (ring/plate) at the end of the throat, a foldable funnel-shaped outlet, and a foldable bioprosthesis sutured inside the end of the funnel (or any other valve mechanism) will be collapsed and mounted onto a balloon catheter and fitted within a flexible introducer sheath. The sheath-covered system will be advanced through the stenosed aortic valve orifice with or without predilatation (Figure 9A). Continuous withdrawal of the sheath will first allow the distal umbrella to unfold (Figure 9B and C), and then the distal umbrella and the funnel-shaped outlet (Figure 9D through F). Inflation of the balloon will expand the stent (throat) of the device and anchor the distal umbrella against the proximal umbrella (Figure 9G). Removal of the balloon concludes the procedure of deployment giving way to blood flow.

In accordance with the described mode of deployment transarterial deployment is possible via a purely percutaneous route (preferable for the femoral, brachial, or transaxillar approach), or through a small surgical incision or mini-thoracotomy (e.g. for the subclavian, innominate artery approach).

3.8 Material of device

The proposed mode of deployment allows for the use of the following materials: selecting a material from the group consisting of a pure metal, a metal alloy, and, combinations thereof. Examplary pure metals are tungsten, platinum, and titanium. Examplary metal alloys are nitinol and stainless steel. For example, metals possessing the required physical properties include (but are not limited to) stainless steel 316 and Nitinol (Nickel Titanium), both of which are biocompatible metals that are commercially available. For example, wires of both materials can be obtained from Allvac Inc, Monroe, NC. Nitinol (Nickel Titanium also possibly obtained from Naval Ordnance Laboratory) may be used for the whole system (excluding the bioprosthesis). Another example is that Nitinol may be used for the umbrellas and the funnel-shaped outlet, and any other conventional metallic stent material other than Nitinol, such as stainless steel 316, for the throat segment. Dacron is typically used for covering Nitionol-based devices, but any other biocompatible surface can be used for coating.

3.9 Use of device without attached valve

The invented pressure recovering device for transarterial implantation into a stenosed aortic valve can also be used without an attached valve in two ways described below

3.91 Use of device without any valve

As demonstrated in Figure 4, the design of the invented device reduces head loss to a minimum even when the cross-sectional area of the throat is only 0.5 cm^2. Flow reversal during diastole will cause flow contraction downstream of the funnel (which in diastole becomes the flow inlet), reducing the effective orifice area substantially. The degree of flow contraction will depend on the angle alpha by which the walls of

the funnel deviate from a straight line, and will vary from 0.5 to 0.8. Assuming a coefficient of contraction (Cc) of 0.6, regurgitant orifice are will be only 60% of the actual cross-sectional throat area (Figure 10). In the example from Figure 4 this will cause a regurgitant orifice of only 0.3 cm^2, which correspond to a regurgitant severity of degree II only. Thus the device will function as a pressure recovering apparatus in systole and a regurgitation minimizing apparatus in diastole.

3.92 Use of device in conjunction with separately implanted prosthesis
Alternatively, a prosthesis can be implanted separately, e.g. into the descending aorta percutaneously as suggested and performed previously, in order to prevent regurgitation, and the invented device will then be implanted separately into the obstructed aortic valve as a pressure recovering apparatus.

4. Summary

The invented device can be implanted percutaneously into a native obstructed aortic valve, typically a calcified one a (but suitable for any etiology of aortic valve disease), without obstructing coronary blood flow or impairing the structural or functional integrity of the surrounding tissues (mitral leaflets, ventricular septum). It allows secure and stable positioning for reliable prevention of device embolism. It allows pressure recovery, minimizing head loss across the aortic valve, providing an optimal hemodynamic profile for any chosen size of cross-sectional flow area at its throat or any size of prosthesis, biological or mechanical, attached to it. It can be used in conjunction with a biological or mechanical prosthesis, either a prosthesis attached to it (as a full aortic valve replacement), or with the prosthesis implanted separately at a remote site downstream. It can also be used without use of an additional prosthesis, since it also operates as a regurgitant orifice area minimizing apparatus.

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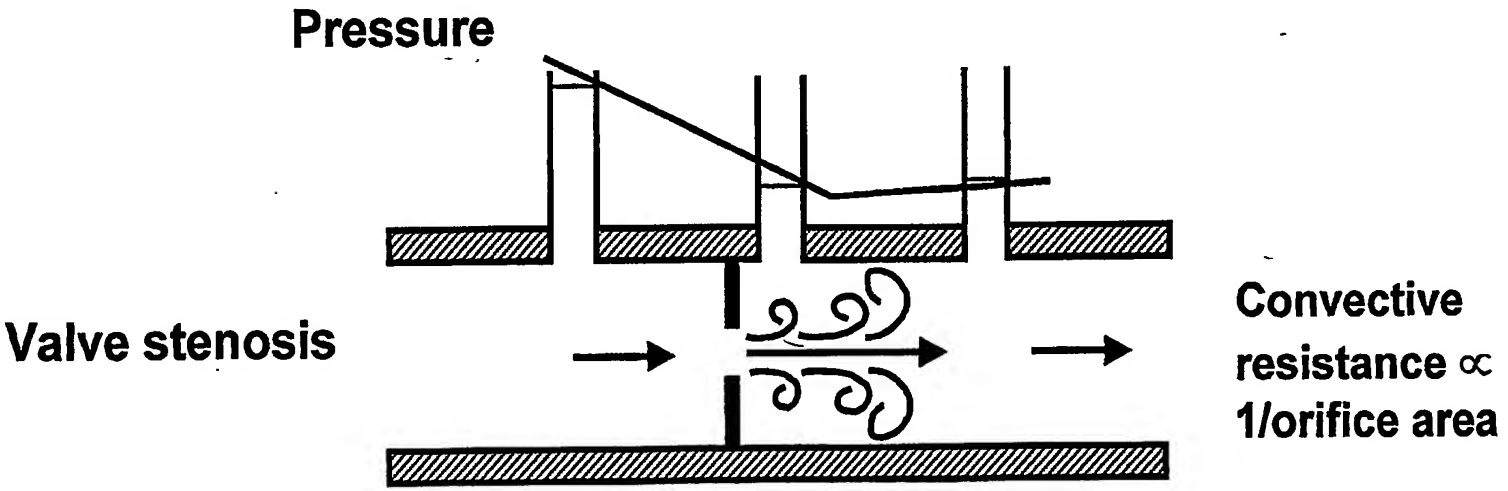
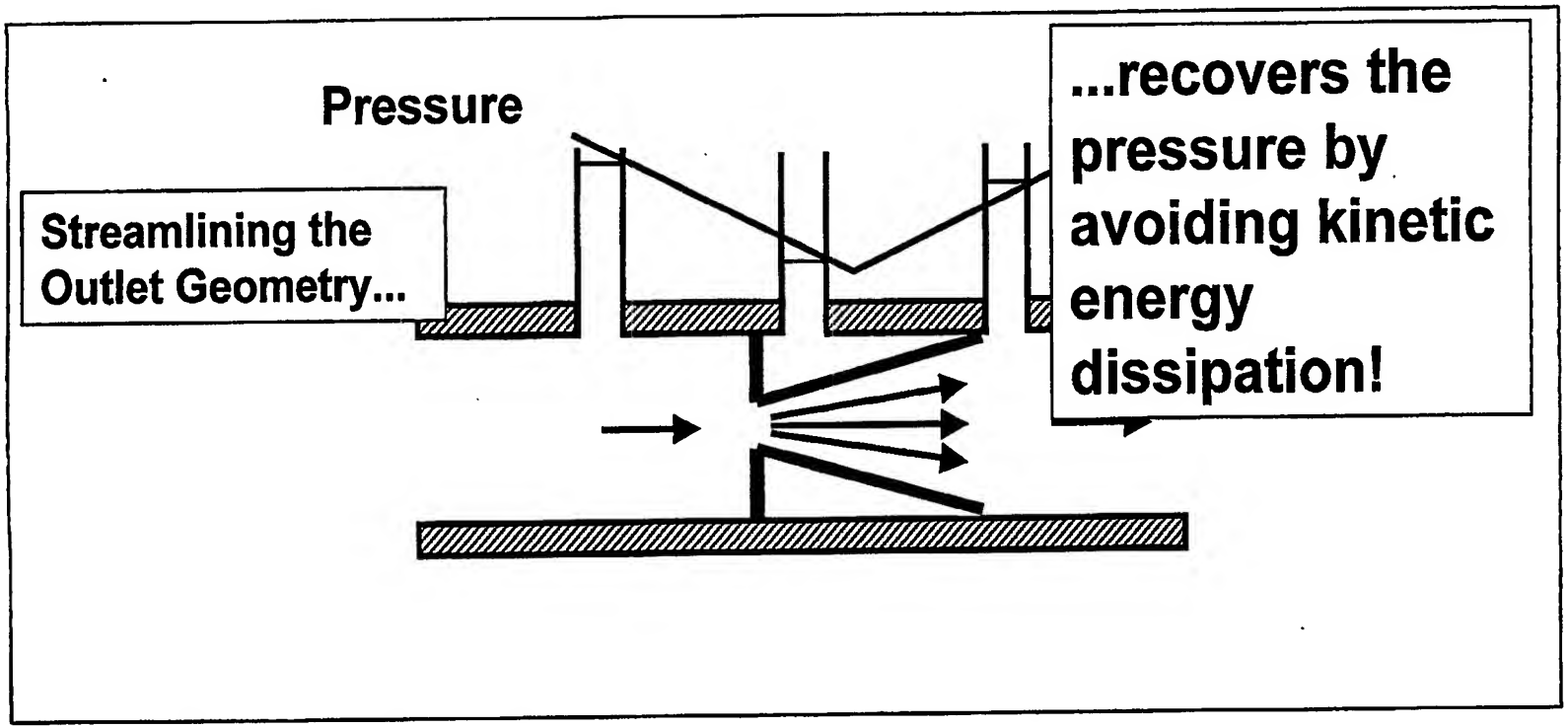
What causes the pressure gradient across a stenotic valve?

By continuity, flow must accelerate at the orifice (increase in kinetic energy, dynamic pressure).Conservation of energy dictates that this is paralleled by a decrease in potential energy (static or lateral pressure).



Most of the kinetic energy is dissipated in turbulence and cannot be reconverted into static pressure

Figure 1



Streamlining the outlet geometry as in a well-designed Venturi meter can reduce the head loss to only 15%, because gradual expansion downstream of the throat eliminates flow separation and allows to recover 85% of the pressure drop.

Figure 2

Similarity Between Oil-Pipeline and Cardiovascular System

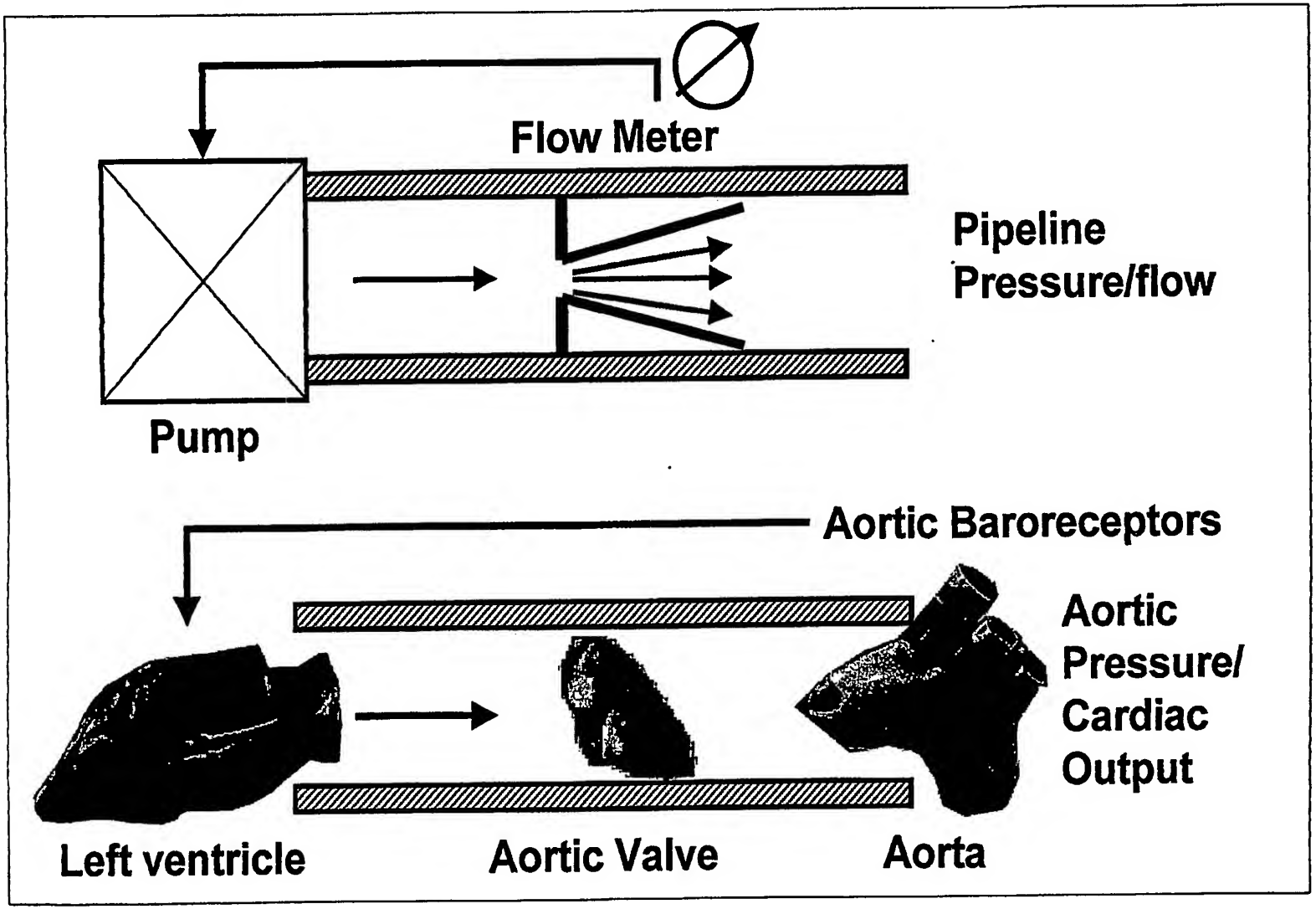
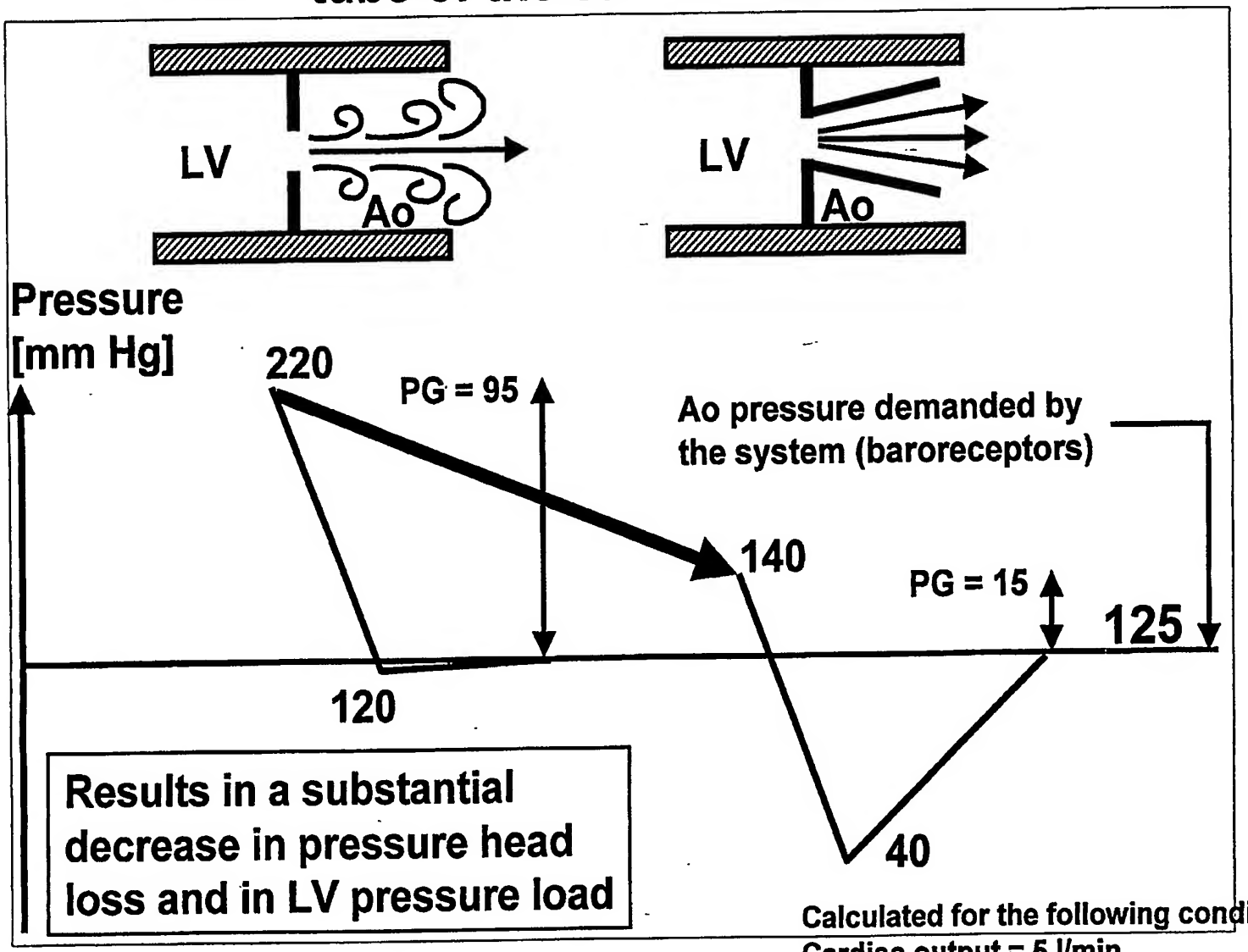


Figure 3

Effect of Replacing a stenotic valve orifice by a Venturi tube of the same throat size



Calculated for the following conditions:
Cardiac output = 5 l/min
cross sectional area of throat = 0.5 cm^2
pressure gradient = 100 mm Hg

Figure 4

Design of Stent of a Valve Prosthesis for Catheter Based Deployment I

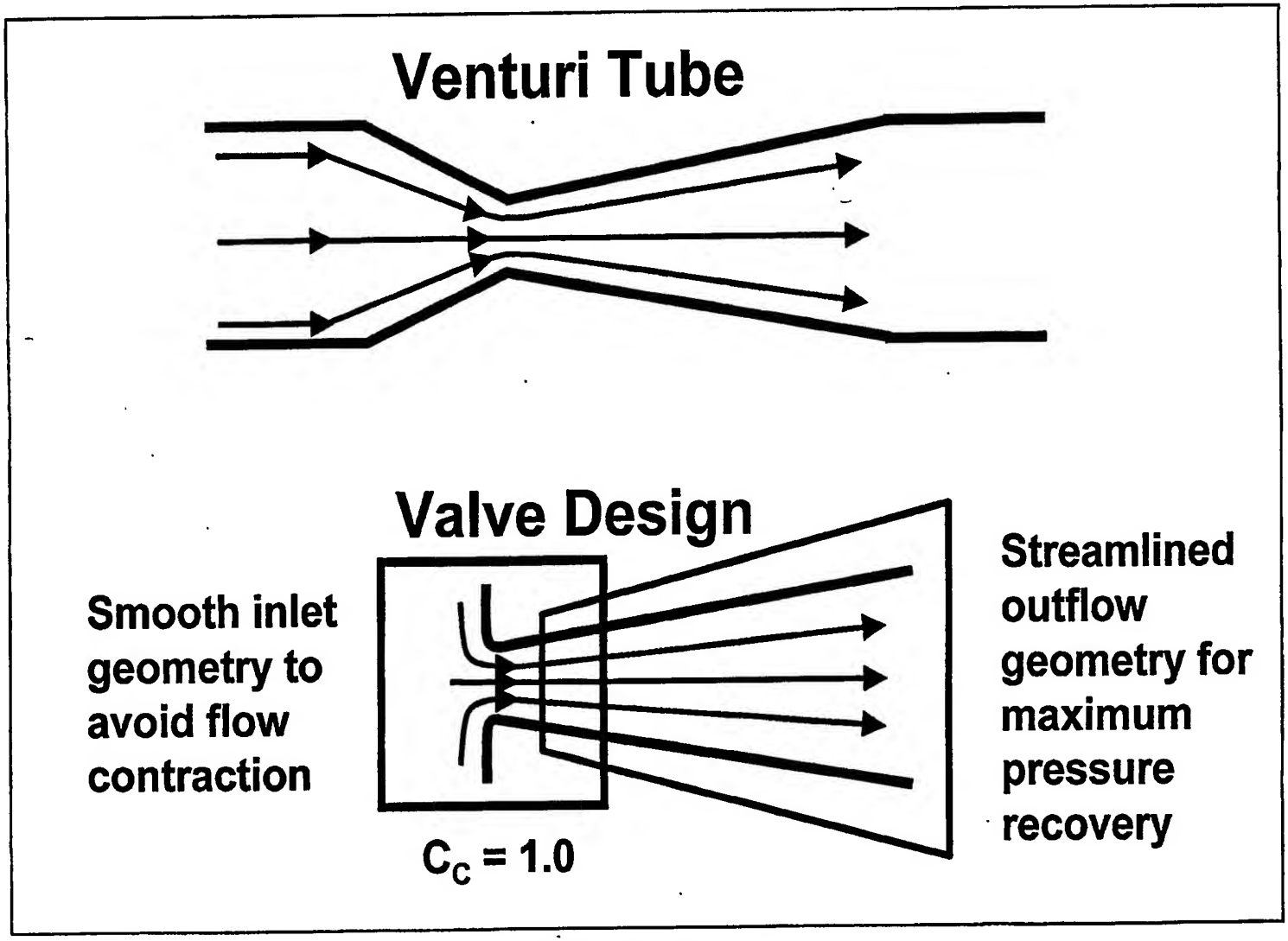


Figure 5

Design of Stent of a Valve Prosthesis for Catheter Based Deployment I

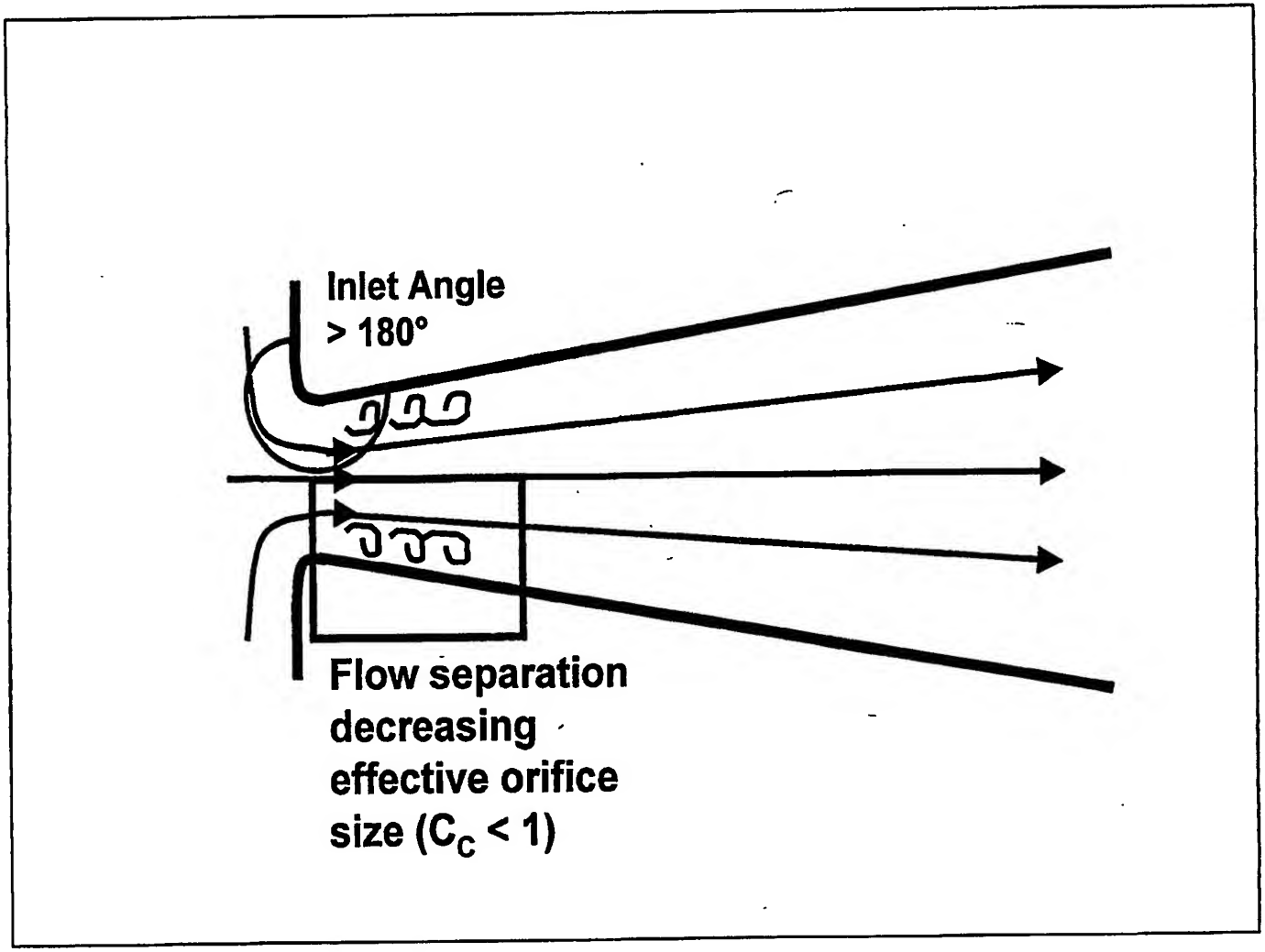


Figure 6

Design of Stent of a Valve Prosthesis for Catheter Based Deployment II

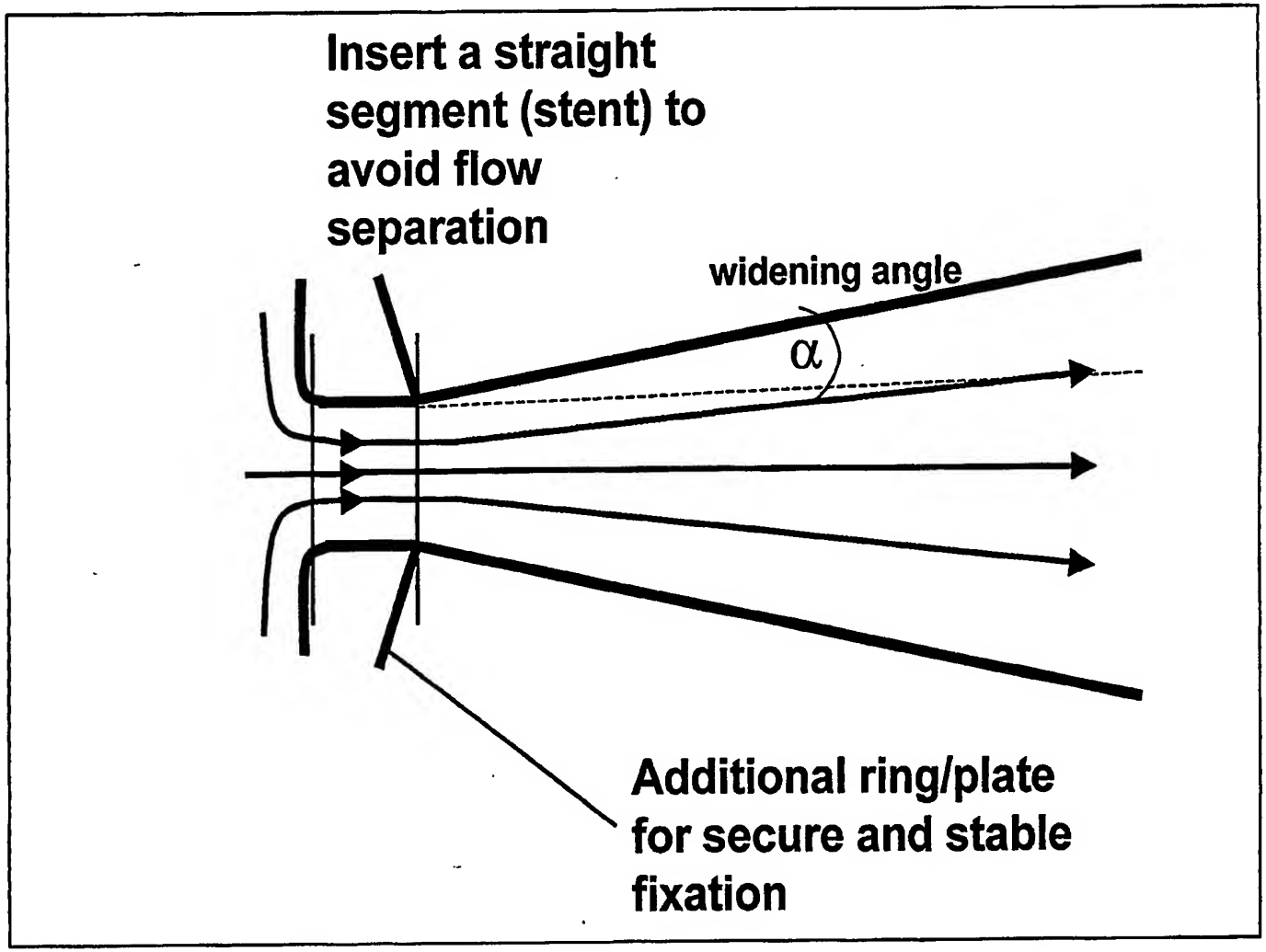


Figure 7

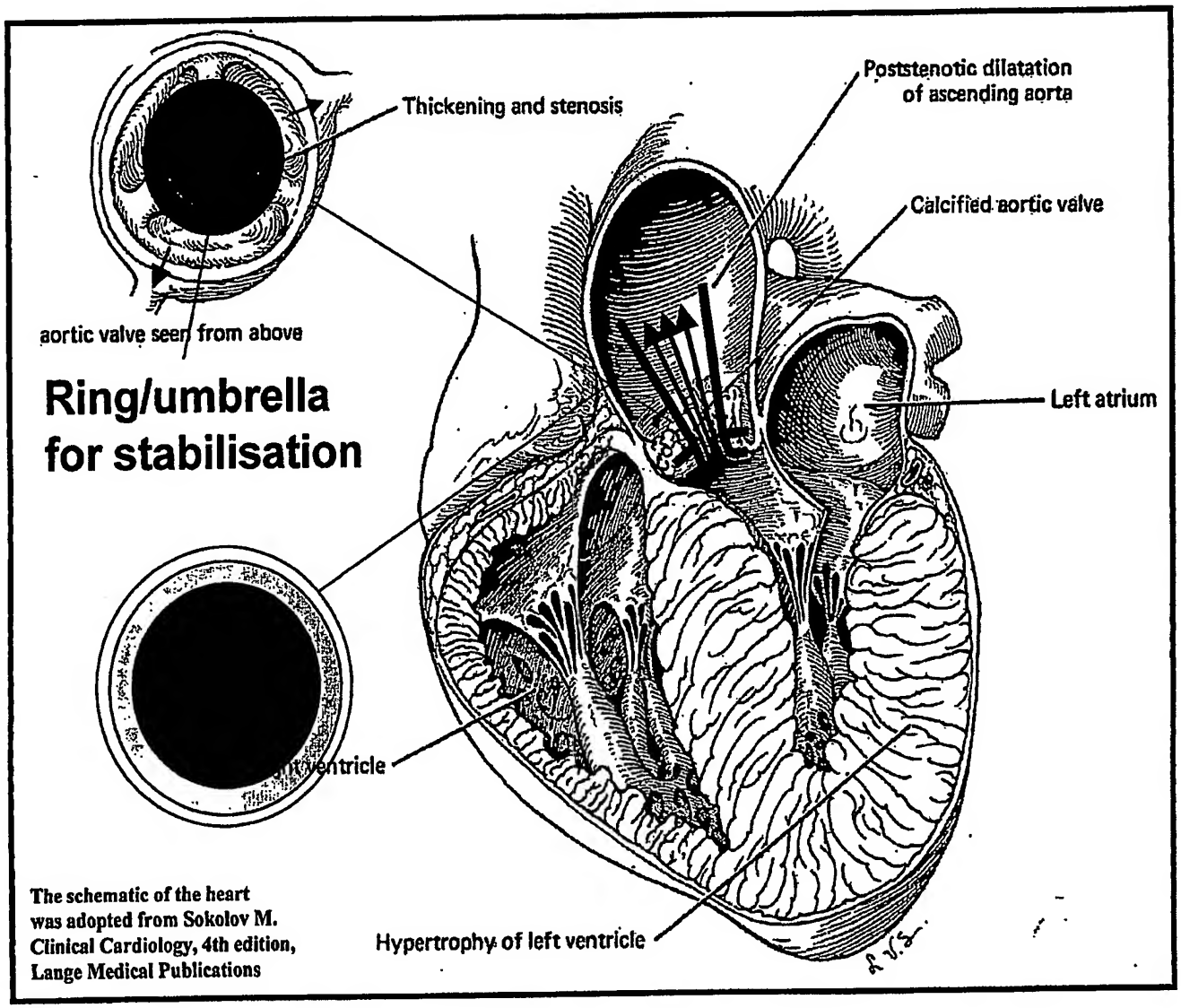


Figure 8

Possible Mode of Deployment I

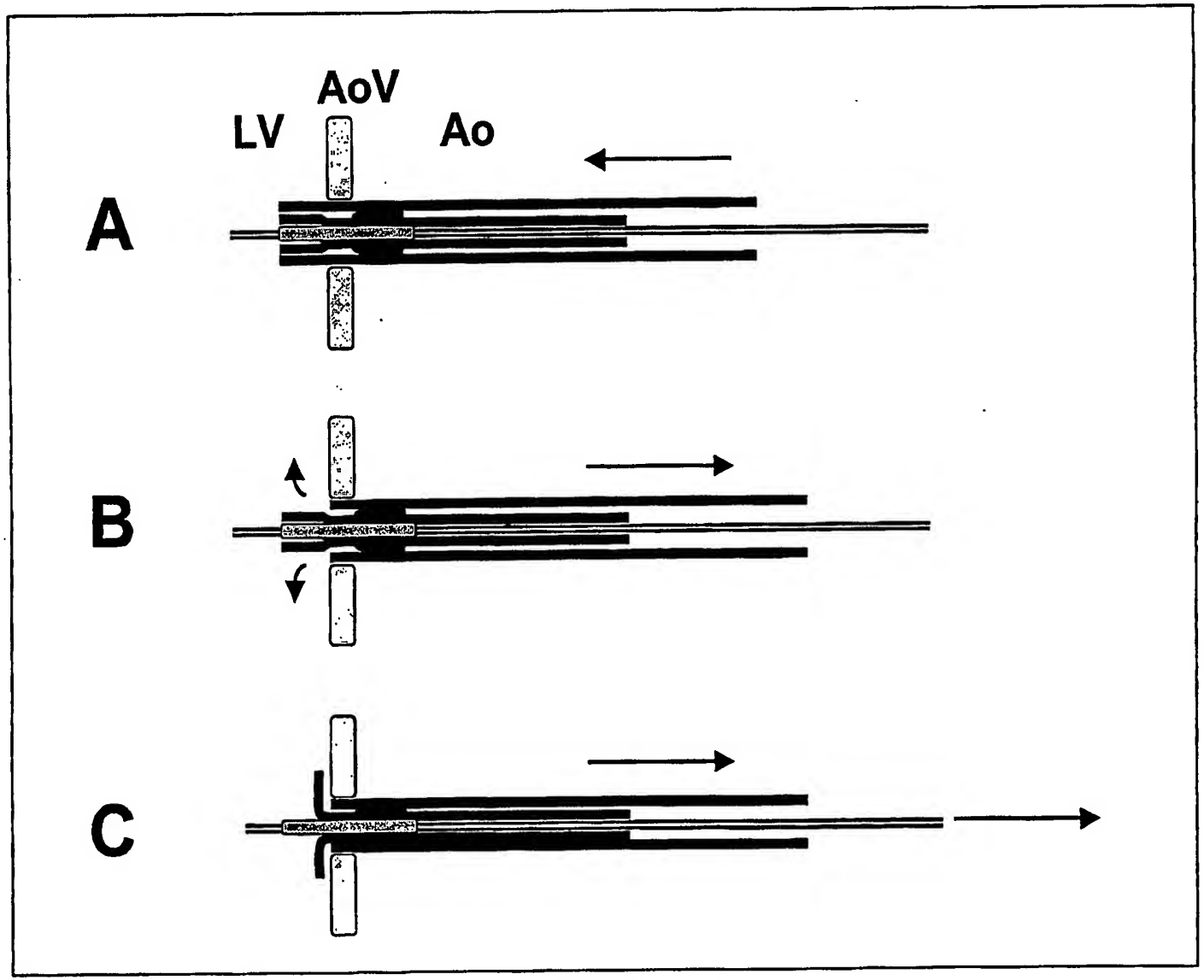


Figure 9 (A - C)

Possible Mode of Deployment II

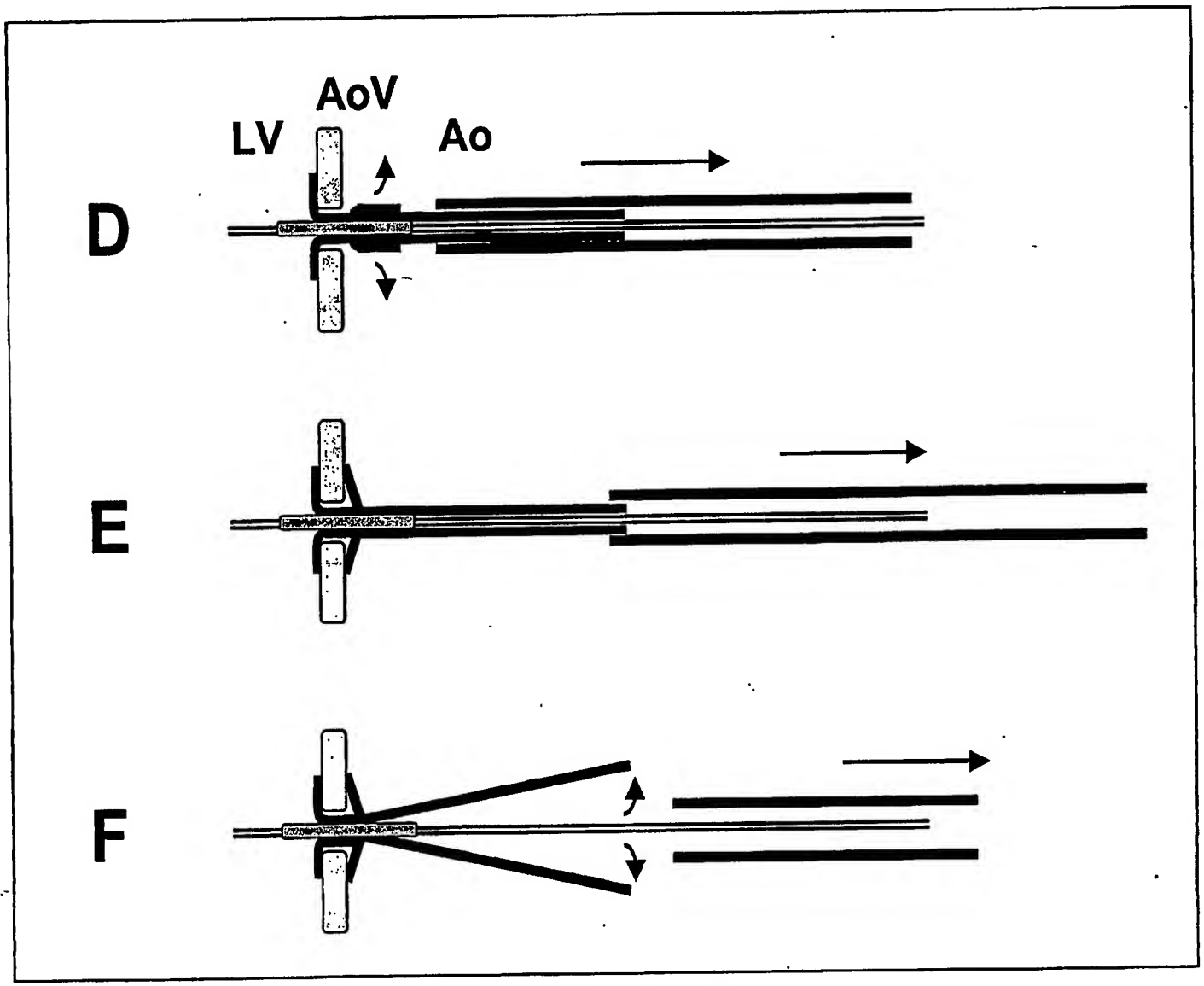


Figure 9 (D - F)

Possible Mode of Deployment III

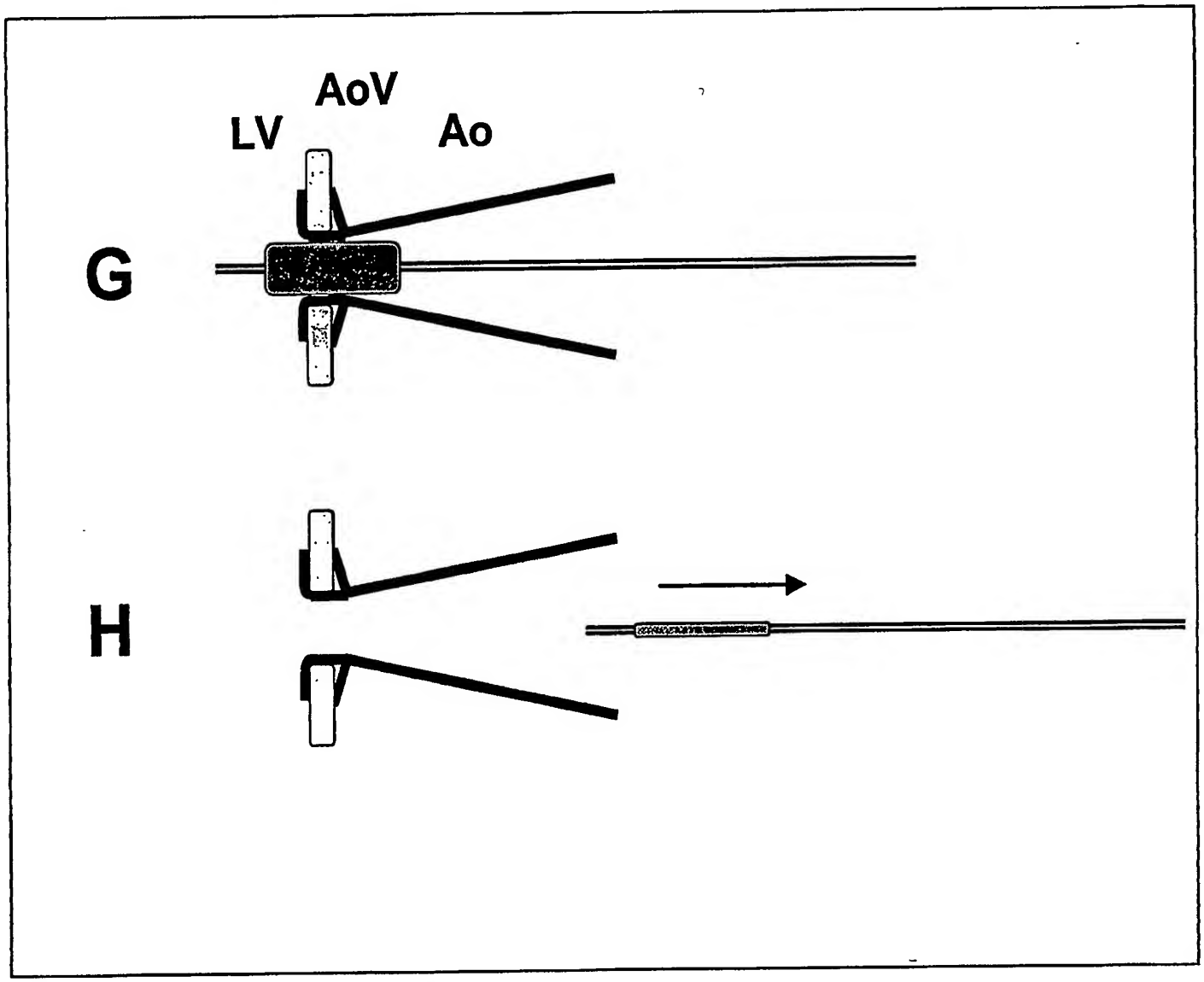


Figure 9 (G, H)

Systole

Cc = 1.0

Diastole

Cc = 0.6

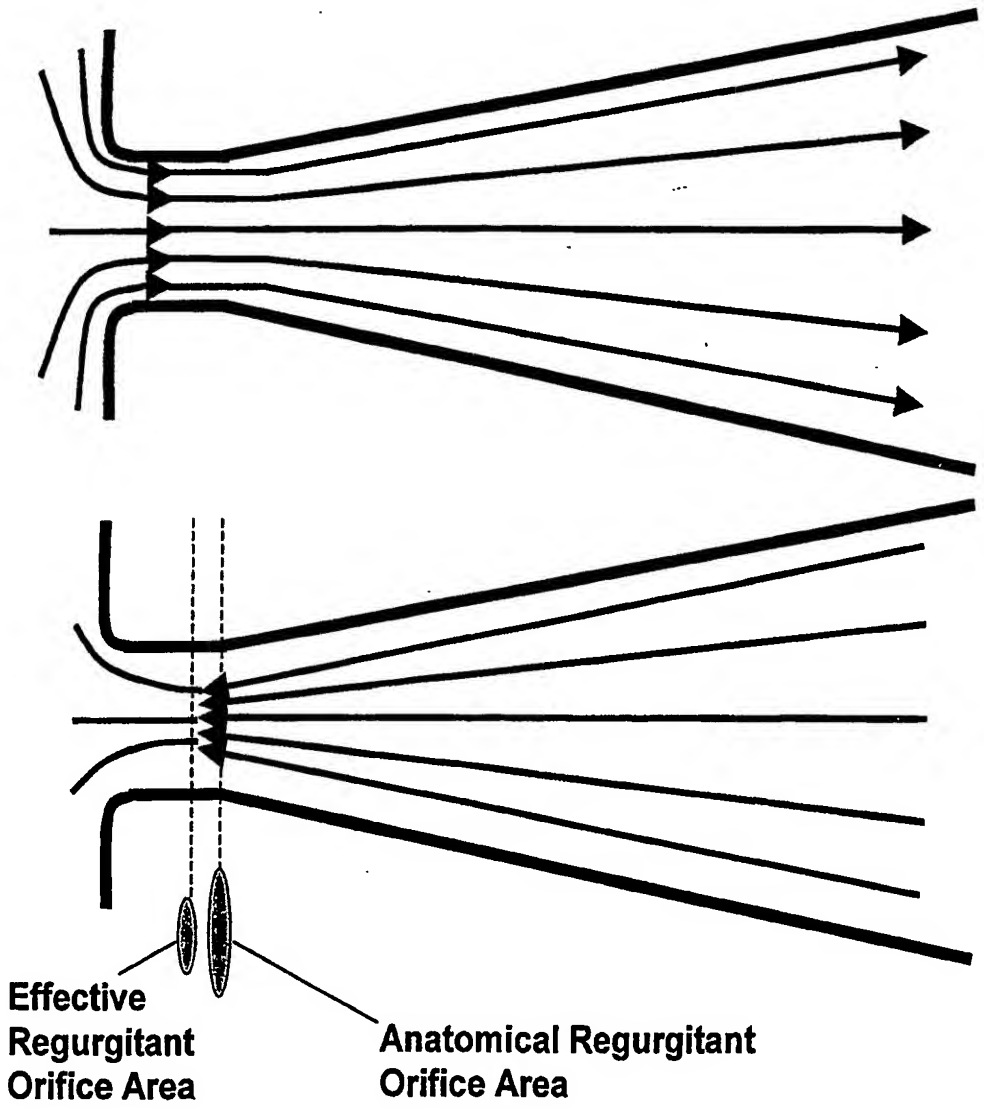


Figure 10

Smooth inlet geometry allows in systole for a coefficient of contraction of 1.0, while in diastole the funnel causes flow contraction, so that effective regurgitant orifice area can be reduced to only 60% of the actual cross sectional throat area